CLAIMS

What is claimed is:

1. A method for delivery of substance through at least one dermal layer, the method comprising:

providing a substance in microcapsules at a predetermined size, within a medium for holding the microcapsules;

placing the medium for holding the microcapsules on a surface of a patch adjacent the skin of a human or animal; and

applying energy to the patch, the energy having a characteristic of disturbing the integrity of the microcapsules, thereby resulting in release of the substance from the microcapsules.

2. The method of claim 1, wherein the energy applied to the patch includes thermal energy.

3. The method of claim 1, wherein the energy applied to the patch includes ultrasonic energy applied to the patch at a resonant frequency for certain or all of the microcapsules, thereby rupturing them.

4. The method of claim 3, wherein the patch includes a top surface which is relatively impermeable to the medium, wherein the medium is surrounded along an outer perimeter with an adhesive matrix, thereby substantially containing the microcapsules within the medium and further substantially containing the substance to be delivered within the patch prior to activation by application of said ultrasonic energy.

5. The method of claim 3, wherein the microcapsules have diameters of approximately 0.003 mm and a resonance frequency of approximately 2000 kHz.

6. The method of claim 3, wherein a rate of release of the substance is controlled in a precise manner by the localized application of the energy.

7. The method of claim 3, wherein certain of the microcapsules have a first resonant frequency and other of the microcapsules have a second resonant frequency, and the release of substance

from the microcapsules is controlled by selective application of ultrasonic energy at the first and at the second resonance frequency.

8. The method of claim 3, wherein:

the substance for delivery is a pharmaceutical substance provided for transdermal drug delivery; and

the substance is activated by a patient controlling the application of the energy.

9. The method of claim 3, wherein said substance includes at least one of: drug, biologically active compound, excipient, skin permeation enhancer.

10. The method of claim 3, wherein said substance includes insulin provided for transdermal delivery.

11. The method of claim 3, wherein said substance includes a vitamin.

12. The method of claim 3, wherein said substance includes skin permeation enhancer.

13. The method of claim 3, wherein the medium for holding the microcapsules includes skin permeation enhancer.

14. The method of claim 1, wherein the energy applied to the patch includes thermal energy.

15. A transdermal patch for infusing active substances into an animal body through the skin comprising:

an inner disc, the inner disc including a encapsulated agents in microcapsules, wherein the microcapsules retain the encapsulated agents prior to activation by energy capable of rupturing the microcapsules;

an outer disc for attachment of the patch to the skin, thereby facilitating contact of the inner disc with a surface of the skin.

16. The transdermal patch of claim 15 wherein the active substance to be infused is a pharmaceutical substance and the pharmaceutical substance is retained prior to infusion in a compatible pharmaceutically-acceptable solvent or excipient vehicle, encapsulated in the microcapsules.

17. The transdermal patch of claim 16 wherein the microcapsules are suspended in a suitable composition, such as pressure-sensitive adhesive, adhesive hydrogel, cream and the like, which contains a permeation-enhancing agent and serves as an outer solvent in which the microcapsules are suspended.

18. The transdermal patch of claim 16 wherein the microcapsules are suspended in a suitable composition, such as pressure-sensitive adhesive, adhesive hydrogel, cream and the like, which contains a permeation-enhancing agent and serves as an outer solvent in which the microcapsules are suspended, and the microcapsules are made of a substance or material that does not permit diffusion into or out of the microcapsule and does not allow leaching out of its contents to any significant extent prior to the application of energy.

19. The transdermal patch of claim 18 wherein the driving force of the pharmaceutical substance for delivery transdermally from the external matrix or vehicle such as pressure-sensitive adhesive, adhesive hydrogel, cream and the like, to the skin is proportional to the difference of the solubility parameter between the pharmaceutical substance to be delivered transdermally and the skin, and between the pharmaceutical substance to be delivered transdermally and the external matrix or vehicle.

20. The transdermal patch of claim 19 wherein a difference between the solubility parameters of the substance to be delivered transdermally and the skin in comparison to the difference between the solubility parameters of the substance to be delivered transdermally and the matrix is minimized in order to maintain a high transdermal flux.

21. The transdermal patch of claim 15 wherein the inner disc includes encapsulated agents in microspheres dispersed in hydrogel.

22. The transdermal patch of claim 15 wherein the inner disc includes encapsulated agents in microspheres dispersed in hydrocolloid.

23. The transdermal patch of claim 15 wherein the inner disc includes encapsulated agents in microspheres dispersed in an aqueous medium in a reservoir type patch.

24. The transdermal patch of claim 15 wherein the microspheres have sizes between 0.01 and 100 micrometers.

25. The transdermal patch of claim 15 wherein the microspheres include polymeric shells.

26. The transdermal patch of claim 15 wherein the microspheres are made of liposomes.

27. The transdermal patch of claim 15 wherein the inner disc includes at least one of: drug, biologically active compound, excipient, skin permeation enhancer.

28. The transdermal patch of claim 15, wherein said substance includes insulin provided for transdermal delivery.

29. The transdermal patch of claim 15, wherein said substance includes vitamin.

30. The transdermal patch of claim 15, wherein said substance includes skin permeation enhancer.

31. The transdermal patch of claim 15, wherein the medium for holding the microcapsules includes skin permeation enhancer.

32. A vehicle and active substance for delivery of the active substance by transdermally partitioning into the skin from an adhesive matrix of a transdermal patch, wherein the active substance is delivered transdermally dependent on a difference in chemical potentials of the

active substance as contained in an external matrix or vehicle and the skin, wherein the active substance is contained within microcapsules which retain the active substance for delivery prior to activation by energy capable of rupturing the microcapsules.

33. The vehicle and active substance of claim 32, wherein unwanted plasticization associated with chemical enhancers and liquid drugs is minimized by maintaining the active substance for delivery in the microcapsules, thereby inhibiting interaction with an adhesive or non-adhesive external matrix or vehicle until their release upon activation.

34. The vehicle and active substance of claim 32, wherein the transdermal patch is manufactured in a pre-activated state, thereby providing enhanced storage stability, and control of release characteristics.

35. The vehicle and active substance of claim 32, wherein:

the substance is a pharmaceutical active substance which is inherently unstable in an aqueous solution or is easily oxidizable; and

the transdermal patch is manufactured in a pre-activated state, thereby providing enhanced storage stability, and control of release characteristics; and the active substance is released in the external matrix on demand by use of the energy in the form of resonance ultrasound or heat.

36. The vehicle and active substance of claim 32 comprising encapsulated agents in microspheres dispersed in a pressure-sensitive adhesive.

37. The transdermal patch of claim 32 wherein the inner disc includes encapsulated agents in microspheres dispersed in hydrogel.

38. The transdermal patch of claim 32 wherein the inner disc includes encapsulated agents in microspheres dispersed in hydrocolloid.

39. The transdermal patch of claim 32 wherein the inner disc includes encapsulated agents in microspheres dispersed in an aqueous, and alcoholic, dialcoholic, and glycerin medium in a reservoir type patch.

40. The transdermal patch of claim 32 wherein the microspheres have sizes between 0.01 and 100 micrometer.

41. The transdermal patch of claim 32 wherein the microspheres include polymeric shells.

42. The transdermal patch of claim 32 wherein the microspheres are liposomes.

43. The transdermal patch of claim 32 wherein the inner disc includes at least one of: drug, biologically active compound, excipient, skin permeation enhancer.

44. The transdermal patch of claim 32, wherein said substance includes insulin provided for transdermal delivery.

45. The transdermal patch of claim 32, wherein said substance includes vitamin.

46. The transdermal patch of claim 32, wherein said substance includes skin permeation enhancer.

47. The transdermal patch of claim 32, wherein the medium for holding the microcapsules includes skin permeation enhancer.

48. A transdermal device containing encapsulated agents in microspheres dispersed in a pressure-sensitive adhesive.

49. A transdermal device containing encapsulated agents in microspheres dispersed in hydrogel.

50. A transdermal device containing encapsulated agents in microspheres dispersed in hydrocolloid.

51. A transdermal device comprising: encapsulated agent in microspheres dispersed in a medium; and alcoholic, dialcoholic and/or glicerin medium in a reservoir type patch.

52. A method of delivering an agent encapsulated in microspheres or nanospheres in a patch matrix comprising the use of ultrasound at a resonant frequency between 0.1 and 100 MHz to rupture the micro or nanospheres, thereby releasing the agent into the patch matrix.

53. The method of claim 52 wherein the agent comprises at least one of: drug, biologically active compound, excipient, skin permeation enhancer.

54. A method of delivering an agent encapsulated in microspheres or nanospheres in a patch matrix comprising the use of heat to melt the spheres, to thereby release the agent.

55. A device with multiple ultrasound sources for selectively rupturing microparticles in a selected area of a patch.

56. A device with multiple heating sources for selectively melting microparticles in a selected area of a patch.

57. The method of the controlled transdermal delivery of an agent as a result of a controlled activation of the given parts of the transdermal patch using an ultrasound source or a heat source.

58. The method of claim 57, wherein the agent comprises insulin.

59. The method of claim 57, wherein the agent comprises vitamin.

60. The method of claim 57, wherein the agent comprises skin permeation enhancer.

61. The method of claim 57, wherein the substance any one or combination of the following:

anti-fungal agent, hormone, vitamin, peptide, enzyme, anti-allergic agent, anti-coagulation agent, antitubercular, antiviral, antibiotic, antibacterial, anti-inflammatory agent, antiprotozoan, local anesthetic, growth factor, cardiovascular agent, diuretic, radioactive compound.

62. The method of claim 61, wherein the substance any one or combination of the following: scopolamine, nicotine, methylnicotinate, mechlorisone dibutyrate, naloxone, methanol, caffeine, salicylic acid, and 4-cyanophenol; anti-fungal agent such as ketoconazole, nystatin, griseofulvin, flucytosine, miconazole, or amphotericin B; hormone such as growth hormone, melanocyte stimulating hormone, estradiol, progesterone, testosterone, cyclomethasone dipropionate, betamethasone, betamethasone acetate and betamethasone sodium phosphate, vetamethasone disodium phosphate, vetamethasone sodium phosphate, cortisone acetate, dexamethasone, dexamethasone acetate, dexamethasone sodium phosphate, flunisolide, hydrocortisone, hydrocortisone acetate, hydrocortisone cypionate, hydrocortisone sodium phosphate, hydrocortisone sodium succinate, methylprednisolone, methylprednisolone acetate, methylprednisolone sodium succinate, paramethasone acetate, prednisolone, prednisolone acetate, prednisolone sodium phosphate, prednisolone tebutate, prednisone, triamcinolone,triamcinolone acetonide, triamcinolone diacetate, triamcinolone hexacetonide and fludrocortisone acetate; a vitamin such as cyanocobalamin neinoic acid, retinoid, retinol palmitate, ascorbic acid, and α-tocopherol, vitamin B-12; peptide; enzyme such as superoxide dismutase or alkaline phosphatase; anti-allergic agent such amelexanox; the anti-coagulation agent such as phenprocoumon or heparin; antitubercular such as paraminosalicylic acid, isoniazid, capreomycin sulfate cycloserine, ethambutolhydrochloride ethionamnide, pyrazinamide, rifampicin, and streptomycin sulfate; the antivirals such as acyclovir, amantadine azidothymidine, ribavirin and vidarabine monohydrate; antibiotic such as dapsone, chloramphenicol, neomycin, cefaclor, cefadroxil, cephalexin, cephradine erythromycin, clindamycin, lincomycin, amoxicillin, ampicillin, bacampicillin, carbenicillin, dicloxacillin, cyclacillin, picloxacillin, hetacillin, methicillin, nafcillin, oxacillin, penicillin G, penicillin V, ticarcillin rifampin and tetracycline; the anti-inflammatory such as diflunisal, ibuprofen, indomethacin, meclofenamate, mefenamic

acid, naproxen, oxyphenbutazone, phenylbutazone, piroxicam, diclofenac, sulindac, tolmetin, aspirin and salicylates; the antiprotozoans such as chloroquine, hydroxychloroquine, metronidazole, quinine and meglumine antimonate; the local anesthetics such as bupivacaine hydrocWoride, chloroprocaine hydrochloride, etidocaine hydrochloride, lidocaine hydrochloride, mepivacaine hydrochloride, procaine hydrocWoride and tetracaine hydrochloride; the growth factors such as Epidermal Growth Factor, acidic Fibroblast Growth Factor, Basic Fibroblast Growth Factor, Insulin-Like Growth Factors, Nerve Growth Factor, Platelet-Derived Growth Factor, Stem Cell Factor, Transforming Growth Factor of the .alpha. family and transforming Growth Factor of the .beta. family; the cardiovascular agents are such as clonidine, propranolol, lidocaine, nicardipine and nitroglycerin; diuretic are such as mannitol or urea; and wherein the radioactive particles are